Non-Technical Abstract

GM-CSF secreting leukemia cell vaccinations after allogeneic non-myeloablative peripheral blood stem cell transplantation in patients with advanced myelodysplastic syndrome or refractory acute myeloid leukemia

This pilot trial will investigate the use as therapeutic vaccines of autologous, irradiated myeloblasts (leukemia cells) engineered by adenoviral mediated gene transfer to secrete human granulocyte-macrophage colony stimulating factor (GM-CSF) in patients with advanced myelodysplasia or resistant acute myeloid leukemia (cancers of the white blood cells) following bone marrow transplantation.

Bone marrow transplantation is a potentially curative therapy for some patients with hematologic cancers. In this approach, the patient's blood forming system (which contains the leukemia) is replaced with a healthy system from an immunologically matched, normal donor. One major way that the transplant destroys the leukemia is through immune-mediated killing by the healthy donor blood cells. The recent development of less toxic regimens (reduced intensity conditioning peripheral blood stem cell transplantation) has now made a larger number of patients eligible for this treatment. However, disease relapse remains the most frequent cause of treatment failure for patients with aggressive blood cancers, especially advanced myelodysplasia and acute myeloid leukemia. One strategy to augment the efficacy of transplantation involves cancer vaccinations. Indeed, our pre-clinical experiments in murine tumor models demonstrated that vaccination with irradiated tumor cells engineered to secrete GM-CSF, following bone marrow transplantation, stimulated potent anti-tumor immunity without significant toxicity. Furthermore, an ongoing phase I study in non-transplanted acute myeloid leukemia patients has already demonstrated that this vaccination strategy is safe, and can stimulate anti-tumor immunity.

In this pilot clinical trial, we will investigate the feasibility, safety, and biologic activity of GM-CSF secreting autologous tumor cell vaccines for patients with refractory myeloid leukemias following reduce intensity conditioning peripheral blood stem cell transplantation. A total of up to 24 patients will be enrolled in the study. Vaccines will be manufactured using a standard first generation adenoviral vector engineered to express GM-CSF and leukemia cells harvested prior to transplantation. Patients will initiate vaccination between days 30 to 45 after transplant, depending upon how quickly the new blood forming system is established. A total of six vaccines (from $1x10^6$ to $1x10^7$ cells per dose, depending upon overall manufacturing yield) will be administered under the skin at weekly (times three) and then every other week intervals (times three). Standard clinical and laboratory measurements of toxicity will be made. A series of laboratory studies will be undertaken to evaluate the immune response stimulated by vaccination.